

Prescribing Tip No: 348 Date: 10<sup>th</sup> February 2022

**Prescribing tip for information**

**EMIS web protocol.  
Trimethoprim and Methotrexate: never co-prescribe.**

A number of prescribing tips have been circulated over recent years highlighting to practices **the potentially fatal interaction** which can occur when patients are concurrently prescribed methotrexate and trimethoprim. **EMIS Web also highlights this drug interaction with a high severity warning.** Despite these warnings we continue to receive reports from colleagues of instances in which these medicines have been co-prescribed.

**Prescribers are advised**

- There is an increased risk of haematological toxicity when methotrexate is given with trimethoprim (also with co-trimoxazole). This **potentially fatal interaction can occur even with short courses or low doses of trimethoprim.**
- Several cases of **severe bone marrow depression (some of which were fatal)** have been reported in patients given low-dose methotrexate and trimethoprim or co-trimoxazole (sulfamethoxazole with trimethoprim).
- Bone marrow suppression can occur abruptly, leading to:
  - Life threatening infections, as the body cannot produce leukocytes in response to invading bacteria and viruses.
  - Anaemia due to a lack of red blood cells.
  - Spontaneous severe bleeding due to a deficiency of platelets.
- Pancytopenia has also been reported in a few patients given co-trimoxazole shortly after stopping methotrexate

The Medicines Optimisation Team have worked together with IT colleagues to devise a prescribing protocol which will flag the following reminder information should any prescriber inadvertently attempt to prescribe trimethoprim / trimethoprim containing medication concurrently to a patient being treated with methotrexate.

**WARNING! Severe interaction between TRIMETHOPRIM and METHOTREXATE**  
**Co-prescribed trimethoprim and methotrexate increases the risk of haematological toxicity and bone marrow depression.**  
**This can lead to life threatening infection, anaemia, and spontaneous severe bleeding. Manufacturer advises AVOID**  
**Severity of interaction: Severe (potentially fatal)**

**The team will work with all practices to install the protocol on the EMIS web clinical system unless otherwise advised.**

**Points to remember**

- 1) Never prescribe trimethoprim (or co-trimoxazole, which contains trimethoprim) to patients receiving methotrexate, not even a short course or a low dose.
- 2) Ensure that details of all '**hospital only issued medications**' are entered onto the patient's clinical record. **If staff do not possess the correct permissions to enter a medication this should be flagged as a priority to an appropriate member of practice staff. It is important to ensure records are always complete and up to date.**
- 3) Ensure all patients on methotrexate have a National Patient Safety Agency methotrexate booklet or a blue Monitoring Disease Modifying Drugs book.
- 4) Be aware that this interaction has been noted in some patients who have recently stopped taking methotrexate.

To contact the Medicines Optimisation Team please phone 01772 214302

If you have any suggestions for future topics to cover in our prescribing tips, please contact [Nicola.schaffel@nhs.net](mailto:Nicola.schaffel@nhs.net)